

Replace the paragraph from page 14, line 27, through page 15, line 2, with:

B2
Amplification of the transmembrane domain of FGFR-4. The following primers were used: sense-GACCGCAGCAGCGCCCGAGGCCAG [SEQ ID NO: 5]; anti-sense AGAGGGAAGAGGGAGAGCTTCTG [SEQ ID NO: 6]. For the PCR reaction, the following were used: 1.5 U/25 μ l Taq-Polymerase (Boehringer, Mannheim) and reaction buffer according to the manufacturer's instructions: 200 μ M dNTP's; 0.2 pmol each of sense and α -sense primer, 0.5 μ l cDNA or genomic DNA from tumour biopsies and cell lines; the following reaction steps were performed: 35 cycles, 95°C 45 secs, 72°C 45 secs.

Replace the paragraph beginning at page 15, line 15, with:

B3
Genotype analysis of genomic DNA by restriction digestion.

Genomic DNA from the tissue samples of the primary tumours was isolated by standard methods (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., 1995). In order to be able to genotype analyse the genomic DNA, the transmembrane region in the FGFR-4 gene was amplified with the following primers in a PCR reaction: 5'-GACCGCAGCAGCGCCCGAGGCCAG-3' (bp 1129-1142; [SEQ ID NO: 5]), and 5'-AGAGGGAAGAGGGAGAGCTTCTG-3' (bp 1275-1297; [SEQ ID NO: 6]). For the PCR reaction, Ready-to-Go PCR Beads (Pharmacia, Uppsala, Sweden) were used. The following PCR cycles were used: 3 min at 95°C, 45 secs at 94°C, 45 secs at 72°C and 5 mins at 72°C. A total of 35 cycles were performed. The PCR products were incubated for 1 hr at 60°C with 5 U/25 μ l of BstN1 (NEB, Schwalbach/Taunus). The DNA fragments from the restriction digestion were separated with a 20% polyacrylamide gel and stained with ethidium bromide. The ³⁸⁸Arg allele is characterized by two fragments of 80 and 29 bp size, while the ³⁸⁸Arg allele is indicated by a single 109 bp sized fragment. Each genotype analysis was repeated three times.

Replace the paragraph from page 15, line 30, through page 16, line 8, with:

B4
DNA sequencing of PCR products. For the sequence analysis of the transmembrane domain of FGFR-4, the PCR products were cloned into the Bluescript vector. For this, a PCR reaction was performed as already described. The following primers were used: sense-GGGAATTCGACCGCAGCAGCGCCCGAGG [SEQ ID NO: 7]; α -sense-GCTCTAGAAGAGGGAAGAGGGAGAG [SEQ ID NO: 8]. The PCR products of the cloning of FGFR-4^{Arg388}/wt could be directly sequenced in the vector pcDNA3. The DNA sequencing of plasmid DNA was performed by the chain termination method. After annealing of the T/-primer onto the plasmid DNA, the sequencing reaction was performed with T/-DNA polymerase (Pharmacia, Freiburg). The products of the sequencing reaction